PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
KLP/BM45417		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP00/09495	26/09/2000	30/09/1999
International Patent Classification (IPC) or national classification and IPC C12N15/31		
Applicant SMITHKLINE BEECHAM BIOLOGICALS S.A. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 4 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
04/04/2001	04.01.2002
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Roscoe, R Telephone No. +49 89 2399 2554

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP00/09495

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:
Description, pages:

1-70 as originally filed

Claims, No.:

1-29 as received on 26/11/2001 with letter of 23/11/2001

Drawings, sheets:

1/45-45/45 as originally filed

Sequence listing part of the description, pages:

1-11, as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☒ contained in the international application in written form.
- ☒ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-29
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-29
Industrial applicability (IA)	Yes:	Claims	1-29
	No:	Claims	

2. Citations and explanations
   see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

V. Reasoned statement on Novelty, Inventive Step and Industrial Applicability

The documents mentioned in the present written opinion / International Preliminary Examination Report are numbered as in the search report, i.e. D1 corresponds to the first document of the search report etc.

- **Novelty (Art.33(2) PCT)**

None of the cited prior art documents provide sequences with significant similarity to those of the application.

Applicants attention is however drawn to section VIII, where clarity problems are identified which effectively lead to a lack of novelty. The claims are considered novel under the proviso that these clarity problems are removed.

- **Inventive Step (Art.33(3) PCT)**

Applicants contribution to the art is the provision of a protein of Moraxella catarrhalis which could find use in a vaccine. Applicant has no idea of the function of the protein, neither has he provided any evidence of practically relevant antigenicity (applicant merely shows that the protein is surface-exposed and a putative lipoprotein). All examples relating to antigenicity are entirely hypothetical. Hence applicant has not solved any problem at the time of filing of the application apart from the provision of a further M. catarrhalis protein that may be suitable for use in a vaccine. It is entirely trivial for a skilled person to isolate a protein from M. catarrhalis which may be useful in vaccination (he does not need any specific prior art instruction to do so but could simply use techniques in any laboratory manual). It may later turn out that the protein is useful in the context of vaccination, yet applicant has not completed the invention in this respect at the time of filing. Hence, claims 1-26 are considered to lack inventive step.
Vast numbers of prior art documents demonstrate the random isolation of genes / proteins from bacteria. Further, a simple database search shows over 50 documents relating to Moraxella antigens before the priority date of the present application (and that is only in a patent literature database). Applicant clearly knows this and cites several documents dealing with Moraxella antigens himself

(p.3 of application). D1 discloses a Moraxella antigen too. Starting from such a prior art, problem is to find any further Moraxella antigen. Solution lies in use of standard screening methods.

- **Industrial Applicability (Art.33(4) PCT)**

No function of BASB132 has been shown and it is not proven that the protein can be put to any practical use apart from in assays for the recognition of the presence of Moraxella and in the production of matter usefull for the diagnosis thereof. Nevertheless, in the case of a bacterial protein this suffices. Hence, the present claims are industrially applicable.

VIII. **Certain observations**

- **Clarity (Art.6 PCT)**

Claim 19 - It is not entirely clear how the membrane expresses a polypeptide (claim 18 also is problematic, particularly because it was the cell rather than the fraction that originally expressed polypeptide - i.e. problem of added matter !). Also claims 18 and19 not novel or at best obvious (i.e. simply isolation of a subcellular fraction (containing e.g. chromosomal gene) or membrane from Moraxella).

Claim 25 - antibody can bind to undefined aa sequences, or even in claim 6 to other part of fusion protein. Clearly, can thus be basically any antibody. Product-by-process definition not acceptable as does not impart novel properties.

Claim 26 - as consequence of cl. 25 can be diagnosis via any Moraxella antigen. Similar problem applies to claim 29.

CLAIMS:

1. An isolated polypeptide comprising an amino acid sequence which has at least 85% identity to the amino acid sequence selected from the group consisting of: SEQ ID NO:2 and SEQ ID NO:4, over the entire length of SEQ ID NO:2 or SEQ ID NO:4 respectively.

2. An isolated polypeptide as claimed in claim 1 in which the amino acid sequence has at least 95% identity to the amino acid sequence selected from the group consisting of: SEQ ID NO:2 and SEQ ID NO:4, over the entire length of SEQ ID NO:2 or SEQ ID NO:4 respectively.

3. The polypeptide as claimed in claim 1 comprising the amino acid sequence selected from the group consisting of: SEQ ID NO:2 and SEQ ID NO:4.

4. An isolated polypeptide of SEQ ID NO:2 or SEQ ID NO:4.

5. An immunogenic fragment of the polypeptide as claimed in any one of claims 1 to 4 in which the immunogenic activity of said immunogenic fragment is substantially the same as the polypeptide of SEQ ID NO:2 or SEQ ID NO:4.

6. A polypeptide as claimed in any of claims 1 to 5 wherein said polypeptide is part of a larger fusion protein.

7. An isolated polynucleotide encoding a polypeptide as claimed in any of claims 1 to 6.

8. An isolated polynucleotide comprising a nucleotide sequence encoding a polypeptide that has at least 85% identity to the amino acid sequence of SEQ ID NO:2 or 4 over the entire length of SEQ ID NO:2 or 4 respectively; or a nucleotide sequence complementary to said isolated polynucleotide over the entire length of said polynucleotide.

9. An isolated polynucleotide comprising a nucleotide sequence that has at least 85% identity to a nucleotide sequence encoding a polypeptide of SEQ ID NO:2 or 4 over the entire coding region; or a nucleotide sequence complementary to said isolated polynucleotide over the entire length of said polynucleotide.

10. An isolated polynucleotide which comprises a nucleotide sequence which has at least 85% identity to that of SEQ ID NO:1 or 3 over the entire length of SEQ ID NO:1 or 3 respectively; or a nucleotide sequence complementary to said isolated polynucleotide over the entire length of said polynucleotide.

11. The isolated polynucleotide as claimed in any one of claims 7 to 10 in which the identity is at least 95% to SEQ ID NO:1 or 3.

12. An isolated polynucleotide comprising a nucleotide sequence encoding the polypeptide of SEQ ID NO:2 or SEQ ID NO:4.

13. An isolated polynucleotide comprising the polynucleotide of SEQ ID NO:1 or SEQ ID NO:3.

14. An isolated polynucleotide comprising a nucleotide sequence encoding the polypeptide of SEQ ID NO:2, SEQ ID NO:4 obtainable by screening an appropriate library under stringent hybridization conditions with a labeled probe having the sequence of SEQ ID NO:1 or SEQ ID NO:3 or a fragment thereof.

15. An expression vector comprising an isolated polynucleotide according to any one of claims 7 - 14.

16. A recombinant live microorganism comprising the expression vector of claim 15.

17. A host cell comprising the expression vector of claim 15.

18. A subcellular fraction of the host cell of claim 17 which subcellular fraction expresses an isolated polypeptide comprising an amino acid sequence that has at least 85% identity to the amino acid sequence selected from the group consisting of: SEQ ID NO:2 and SEQ ID NO:4.

19. A membrane of the host cell of claim 17 which membrane expresses an isolated polypeptide comprising an amino acid sequence that has at least 85% identity to the amino acid sequence selected from the group consisting of: SEQ ID NO:2 and SEQ ID NO:4.

20. A process for producing a polypeptide of claims 1 to 6 comprising culturing a host cell of claim 16 under conditions sufficient for the production of said polypeptide and recovering the polypeptide from the culture medium.

21. A process for expressing a polynucleotide of any one of claims 7 – 14 comprising transforming a host cell with the expression vector comprising at least one of said polynucleotides and culturing said host cell under conditions sufficient for expression of any one of said polynucleotides.

22. A vaccine composition comprising an effective amount of the polypeptide of any one of claims 1 to 6 and a pharmaceutically acceptable carrier.

23. A vaccine composition comprising an effective amount of the polynucleotide of any one of claims 7 to 14 and a pharmaceutically effective carrier.

24. The vaccine composition according to either one of claims 22 or 23 wherein said composition comprises at least one other *Moraxella catarrhalis* antigen.

25. An antibody generated against the polypeptide or immunological fragment as claimed in any one of claims 1 to 6.

26. A method of diagnosing a *Moraxella catarrhalis* infection, comprising identifying a polypeptide as claimed in any one of claims 1 - 6, or an antibody that is immunospecific for said polypeptide, present within a biological sample from an animal suspected of having such an infection.

27. Use of a composition comprising an immunologically effective amount of a polypeptide as claimed in any one of claims 1 – 6 in the preparation of a medicament for use in generating an immune response in an animal.

28. Use of a composition comprising an immunologically effective amount of a polynucleotide as claimed in any one of claims 7 - 14 in the preparation of a medicament for use in generating an immune response in an animal.

29. A therapeutic composition useful in treating humans with *Moraxella catarrhalis* disease comprising at least one antibody directed against the polypeptide of claims 1 – 6 and a suitable pharmaceutical carrier.